APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/020,743	02/09/98	MACK	D 018547-03480

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EXAMINER
SIEW, I

ART UNIT	PAPER NUMBER
1634	9

DATE MAILED:

04/13/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

	Application No.	Applicant(s)
	09/020,743	Mack
	Examiner	Group Art Unit
	Jeffrey Siew	1634

☐ Responsive to communication(s) filed on _____ .

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire _____3_____ month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained· under the provisions of· 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-48* _____ is/are pending in the application.

☐ Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-48* _____ is/are rejected.

☐ Claim(s) _____ is/are objected·to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

    ☐ All ☐ Some* ☐ None   of the CERTIFIED copies of the priority documents have been

      ☐ received.

      ☐ received in Application No. (Series Code/Serial Number) _____ .

      ☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

    *Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *5 (2 pgs)*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

The previous office action mailed 3/5 /99 is hereby withdrawn in light of this new

office action.

Drawings

1. This application has been filed with informal drawings which are acceptable for

examination purposes only. Formal drawings will be required when the application is allowed.

Specification

2. The title of the invention is not descriptive. A new title is required that is clearly indicative

of the invention to which the claims are directed.

The following title is suggested: Computer-aided display for Comparative Gene

Expression

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and
> distinctly claiming the subject matter which the applicant regards as his invention.

4.   Claims 1-48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for

failing to particularly point out and distinctly claim the subject matter which applicant regards as

the invention.

A)   Claims 1-48 are confusing because it cannot be determined whether the two axis are

connected.

B)   Claims 1-48 are vague and indefinite because of the terms "position" and "relative" in

claims 1,20,25,44,47 & 48. It cannot be determined what measure is used to define the meaning

of "relative". It is suggested that position be amended to "position with X, Y coordinates where in

the X position is selected relative to the first axis and Y axis etc". For subsequent claims 19 & 43

which involve a third axis, it is suggested to add Z coordinates. The use of these terms would

have been well known and commonly practiced in the art of graphically displaying images.

C)   Claims 1-48 are vague and indefinite because of the term "corresponding". Particularly in

claims 1,20,25,44,47 & 48, it cannot be determined in what way or manner the "correspondence"

is to occur.

D)   Claim 4 recites the language "mark step" and depends on claim 1. However, proper antecedent basis is lacking in claim 1.Claim 4 depends on claim 1 which recites the language of "displaying a mark". However, claim 1 does not recite a "mark step". It cannot be determined what the term is referring to.

E)   Claim 6 recites the language " said monitoring step" and depends on claim 3. However, proper antecedent basis is lacking in claim 3. It cannot be determined to what monitoring step is being referred to.

F)   Claim 25 recites the language "first and second". However, proper antecedent basis is lacking in claim 25 for these terms. It is suggested the claims be amended to include "a first and second".

G)   Claim 6-10 are confusing because it cannot be determined to where the step of inputting is to occur. It cannot be determined whether the input is referring to the probe pair into the samples or the results into a computer for display.

H)   Claim 6 is confusing because it cannot be determined at what point the steps are to be

performed in relationship to the steps in claims 1 & 6. It is suggested that a phrase be included in

the preamble reciting "wherein the comparing step" further comprises".

I)   Claim 10 & 34 are confusing because of the term "pairs that cause" because it cannot be

determined as to what the pairs are to cause.

J)   Claim 9 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for

omitting essential steps, such omission amounting to a gap between the steps. See MPEP

§ 2172.01. The omitted steps are: computing the IDIF between the Ipm-Imm. Clarificaton is

requested.

K)   Claim 10 &34 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete

for omitting essential steps, such omission amounting to a gap between the steps. See MPEP

§ 2172.01. The omitted steps are: averaging the IDEF values. The specification discloses that

the determination of expression is based on several calculations may be used to calculate the

expression level (see page 11, lines 5-14). However in using the calculation of the sum of IDEF

values as recited in claim 10 would necessitate an averaging step.

L)   Claim 11& 35 are confusing because of the phrase "user input selecting said mark" is not grammatically correct. It cannot be determined what the phrase is referring to. It is suggested the phrase be amended to " an input of a user's selection of said mark".

M)   Claims 11,12 & 36 are confusing because of the term "information". It cannot be determined to what or what type of information is to be displayed. The rejection would be overcome if the claims were to be amended to include "comprises a GENBANK accession number".

N)   Claim 17& 41 are confusing because it cannot be determined " treatment strategy". It cannot be determined how a characteristic comprises a " treatment strategy".

O)   Claims 16 & 40 are confusing because of the phrase "presence of disease". Although disease level or state are commonly used, the use of "presence" would more likely refer to an actual physical presence such as a bacteria or virus. It is suggested that the claim be amended to "disease state".

P)   Claim 30 recites the language " said monitoring step" and depends on claim 3. However, proper antecedent basis is lacking in claim 27. It cannot be determined to what monitoring step is being referred to.

Claim Rejections - 35 USC § 102

5.   The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the

basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6.   Claims 1-5, 20,21 & 23 are rejected under 35 U.S.C. 102(b) as being anticipated Zhao et

al (Gene Vol. 156 pp. 207-213 1995).

Claims 1-5, 20,21 & 23 are drawn to displaying expression levels or compound

concentration of two samples on a graph in which the first axis corresponds to expression level of

first sample and the second axis is perpendicular to first axis and corresponds to expression level

of second sample and a mark is displayed.

Zhao et al teach bioimaging analyzer system to compare the expression profiles of

thousands of genes cDNAs) simultaneously . They teach the a high density cDNA filter analysis in

which expression profiles of 2505 cloned human brain cDNAs (genes) were monitored (see whole

document esp. Abstract). A quantitative analysis of the filter is performed using Fuji Bioimaging

Analyzer BAS2000 System and automated quantification program AutoQuant. The final part is

sequence analysis in which each clone is characterized by homology search in the GENBANK

nucleotide Sequence Database (see page 208 & Figure 1). They applied the system for the

comparative analysis of expression profile of the human cDNAs in brain. The expression profiles

were illustrated on graphs by comparing the their scores from two tissues with Microsoft Excel

(Microsoft) on a Macintosh personal computer(see page 210-211 and fig. 3). A mark for each

gene is positioned relative to the expression levels in the two different samples.

Claim Rejections - 35 USC § 103

7.   The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness

rejections set forth in this Office action:

> (a) a patent may not be obtained though the invention is not identically disclosed or described as set forth in
> section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are
> such that the subject matter as a whole would have been obvious at the time the invention was made to a person
> having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the
> manner in which the invention was made.

8.   Claims 25-29,44,45,47 & 48 are rejected under 35 U.S.C. 102(b) as anticipated by or, in

the alternative, under 35 U.S.C. 103(a) as obvious over Zhao et al (Gene Vol. 156 pp. 207-213

1995).

Claims 25-29,44 & 45 are drawn to a software product that contains code that displays on

first axis expression level or compound in first sample, displays on second axis an expression level

or compound in second sample, displays a mark whose position is relative to first or second axis.

Claim 47 is drawn to computer system comprising display, processor and memory for displaying a first axis corresponding to expression level of first axis, code for displaying a first axis corresponding to expression level of first axis and code for displaying a mark , a computer readable storage medium for storing codes.

Claims 48 is drawn to computer system comprising display, processor and memory for displaying a first axis corresponding to a compound concentration, code for displaying a first axis corresponding to compound concentration and code for displaying a mark , a computer readable storage medium for storing codes.

Zhao et al teach bioimaging analyzer system to compare the expression profiles of thousands of genes cDNAs simultaneously . They teach a high density cDNA filter analysis in which expression profiles of 2505 cloned human brain cDNAs (genes) were monitored (see whole document esp. Abstract). A quantitative analysis of the filter is performed using Fuji Bioimaging Analyzer BAS2000 System and automated quantification program AutoQuant. The final part is sequence analysis in which each clone is characterized by homology search in the GENBANK nucleotide Sequence Database (see page 208 & Figure 1). They applied the system for the comparative analysis of expression profile of the human cDNAs in brain. The expression profiles were illustrated on graphs by comparing the their scores from two tissues with Microsoft Excel (Microsoft) on a Macintosh personal computer(see page 210-211 and fig. 3). A mark for each gene is positioned relative to the expression levels in the two different samples. Although the reference is silent to the teaching of "code", it was well known and commonly practiced that

Microsoft Excel (see page 211) is a software product containing code used to generate graphs.

Through the use of this code, Zhao et al generated the graphs depicted in Figure 3 to compare.the

expression level of two different samples. Moreover, the computer used was a Macintosh

computer(see page 211) as depicted in Figure 1. Although the reference is silent to the teaching of

processor, memory and display, the personal computer inherently contains a display,

microprocessor and memory in the form of RAM, ROM and hard disk.

In the alternative one of ordinary skill in the art would have been motivated to implement

the Microsoft Excel program in code format to display the expression level in order to analyze

various data inputs from various samples on different platforms. A program code provides

versatility in allowing dynamic input to be analyzed. It would have been advantageous to

implement analysis and display on code so that a large number of different samples would be

analyzed especially over time. Moreover, the implementation on code would allow the analysis to

be performed across different platforms and even different machines. It would have been prima

facie obvious to implement the display of the expression levels through a computer code

comprising code in order to analyze and display a constantly changing and new input across

different platforms and machines.

Moreover, in the alternative one of ordinary skill in the art would have been motivated to

to display the expression level on a computer system containing display, processor and memory in

order to analyze various data inputs from various samples. A computer system provides excellent

data storage and data manipulation capabilities. It would have been advantageous to implement

analysis and display on a computer system so that a large number of <u>different</u> samples would be

analyzed. It would have been <u>prima facie</u> obvious to implement the display of the expression

levels on a computer system in order to analyze large amounts of data efficiently.

9.   Claim 19 & 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhao et al

(Gene Vol. 156 pp. 207-213 1995).

Claim 19 is drawn to claim 1 with the further limitation of displaying third axis wherein

the mark is position relative to expression level of a third sample.

Claim 43 is drawn to claim 25 a computer product with the further limitation of having

code displaying third axis wherein the mark is position relative to expression level of a third

sample

The teachings or suggestions of <u>Zhao et al</u> are described previously, briefly they teach

bioimaging analyzer system to compare the expression profiles of thousands of genes cDNAs)

simultaneously. They teach the a high density cDNA filter analysis in which expression profiles of

2505 cloned human brain cDNAs (genes) were monitored (see whole document esp. Abstract). A

quantitative analysis of the filter is performed using Fuji Bioimaging Analyzer BAS2000 System

and automated quantification program AutoQuant. The final part is sequence analysis in which

each clone is characterized by homology search in the GENBANK nucleotide Sequence Database

(see page 208 & Figure 1). They applied the system for the comparative analysis of expression

profile of the human cDNAs in brain. The expression profiles were illustrated on graphs by

comparing the their scores from two tissues with Microsoft Excel (Microsoft) on a Macintosh

personal computer(see page 210-211 and fig. 3). A mark for each gene is positioned relative to

the expression levels in the two different samples. Although the reference is silent to the teaching

of "code", it was well known and commonly practiced that Microsoft Excel (see page 211) is a

software product containing code used to generate graphs. Through the use of this code, Zhao et

al generated the graphs depicted in Figure 3 to compare the expression level of two different

samples. Moreover, the computer used was a Macintosh computer(see page 211) as depicted in

Figure 1. Although the reference is silent to the teaching of processor, memory and display, it was

well known and commonly practiced in the art that personal computer contains a display,

microprocessor and memory in the form of RAM, ROM and hard disk.

Zhao et al do not teach a third axis.

One of ordinary skill in the art would have been motivated to apply a third axis to Zhao et

al display format in order to further compare the expression level in a third sample. It would have

been advantageous to use a 3D format to compare three samples at the same time so that

comparisons would be visually easier to interpret and would be performed simultaneously. It

would have been prima facie obvious to apply a third axis to Zhao et al's display format in order

to analyze more information at the same time.

10.   Claims 6-18 & 30-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over

Lockhart et al (WO97/27317 21 July 1997) in view of Zhao et al (Gene Vol. 156 pp. 207-213

1995).

Claims 6-18 are drawn to claim 1 in which the expression level of expressed sequence is

monitored.

Claims 30-42 are drawn to computer product comprising code for displaying a first axis

corresponding to expression level of first axis, code for displaying a first axis corresponding to

expression level of first axis and code for displaying a mark , a computer readable storage medium

for storing codes.

Lockhart et al teach a method of detecting nucleic abundances or concentrations (e.g.

expression levels) between two or more samples (see whole document esp. abstract). They teach

the simultaneous monitoring of the expression of a multiplicity of genes using perfect match probe

and mismatch probes (see page 5,12,47 & esp. 49-50). They teach that expression monitoring

would be useful for both drug safety and toxicology screenings (see page 230) and monitoring

various genes in response to defined stimuli such as drugs (see page 22). They teach that

monitoring of gene expression may be performed using a computer system running a software

program that includes computer code incorporating analysis of hydridization intensities of the

screens(see page 90 & Figure 6-8). They teach a method of comparing expression level using the

hybridization intensities between the perfect match and mismatch probes (see page 93-101 &

Figure 9-10B). They compare the hybridization intensity difference and ratio of the perfect match

and mismatch probes with a threshold. The values NPOS, NNEG and LR are calculated for each

pair of probes. The analysis is repeated to calculate the average of the differences. They teach that

oligonucleotide pairs that show the greatest differential hybridization between two samples can be

identified by sorting the observed hybridization ratio and difference values. Based on identified

oligonucleotide pair sequences, a gene can be searched for in sequence databases such as

GENBANK (see page 128-9). They also display the results in a graph showing differential

expression between samples (see Figures 16-17).

Lockhart et al do not teach presenting expression level information by displaying on a first

axis representing the expression level in a first sample, displaying on second axis representing the

expression level in the second axis and displaying a mark relative to the two axes.

Zhao et al teach bioimaging analyzer system to compare the expression profiles of

thousands of genes cDNAs) simultaneously . They teach the a high density cDNA filter analysis in

which expression profiles of 2505 cloned human brain cDNAs (genes) were monitored (see whole

document esp. Abstract). A quantitative analysis of the filter is performed using Fuji Bioimaging

Analyzer BAS2000 System and automated quantification program AutoQuant. The final part is

sequence analysis in which each clone is characterized by homology search in the GENBANK

nucleotide Sequence Database (see page 208 & Figure 1). They applied the system for the

comparative analysis of expression profile of the human cDNAs in brain. The expression profiles

were illustrated on graphs by comparing the their scores from two tissues with Microsoft Excel

(Microsoft) on a Macintosh personal computer(see page 210-211 and fig. 3).

One of ordinary skill in the art would have been motivated to display the comparative

expression levels of genes as in Zhao et al's to Lockhart et al's analysis technique in order to

compare the gene expression between two different samples. Zhao et al's display format allows

easy visualization of the many different expressions of genes between two samples. It would have

been prima facie obvious to construct a graph with an axis representing the gene expression in one

sample and another axis representing the gene expression in a second sample in order to compare

the differential gene expression between the different samples.

9.   Claims 22, 24 & 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhao

et al in view of Beattie (US5,843,767 December 1, 1998).

Claims 22 & 24 are drawn to claim 20 with the added limitation the polymer is a protein.

Claim 46 is drawn to claim 44, a computer product with the added limitation the polymer

is a protein.

The teachings and suggestions of Zhao et al are described above.

Zhao et al do not teach the use of protein polymers.

Beattie et al teach the use of protein probes such as antibodies in hybridization array (see

whole document).

One of ordinary skill in the art would have been motivated to apply Beattie et al's teaching

of using protein probes to Zhao et al's expression display in order to compare the expression level

of actual translated protein between two samples. Beattie states that the use of antibodies or

ligand receptor binding would be applicable to the study of identifying biomolecules. It was well

known and commonly practiced to use these ligand -receptor binding techniques in order to

actually identify the stage of gene expression i.e. the translated protein. It would have been prima

facie obvious to use Beattie's protein probes and display the results between two samples using

Zhao et al's expression method in order to compare the protein levels which represent the final

stage of gene expression.

10.   Any inquiry concerning this communication or earlier communications from the examiner

should be directed to Jeffrey Siew whose telephone number is (703) 305-3886 and whose e-mail

address is jsiew@uspto.gov. The examiner can normally be reached on Monday through Friday

from 6:30 a.m. to 3 p.m. If attempts to reach the examiner by telephone are unsuccessful, the

examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application or proceeding

should be directed to the receptionist for Technology Center 1600 whose telephone number is

(703) 308-0196.

Papers related to this application may be submitted to Group 1600 by facsimile

transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal

Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette,

1096 OG 30 (November 15, 1989). The CM1 Center numbers for Group 1600 are Voice (703)

308-3290 and Fax (703) 305-3014 or (703) 305-4242.

Art Unit: 1634

Jeffrey Siew

March 29, 1999

KENNETH R. HORLICK
PRIMARY EXAMINER
GROUP 1800 1600   3/29/99